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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HELMS, LARRY RONALD	

ART UNIT	PAPER NUMBER
1642	18

DATE MAILED: 10/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/779,439	NOUJAIM, ANTOINE	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *1-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claim 22 has been amended.

Claims 26-28 have been added.

2. Claims 1-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions. Election was made **without** traverse in Paper No. 10.

3. Claims 22-28 are under examination.

4. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

5. The following Office Action contains NEW GROUNDS of rejection.

Rejections Withdrawn

6. The rejection of claims 22-25 under 35 U.S.C. 103(a) as being unpatentable over Madiyalakan et al (WO 97/42973, published 11/20/97, IDS #5) and further in view of Goletz et al (U.S. Patent 5,997,869, issued 12/99) is withdrawn in view of the new grounds of rejection.

7. The rejection of claims 22-25 under 35 U.S.C. 103(a) as being unpatentable over Madiyalakan et al (U.S. Patent 6,241,985, filed 3/20/98, IDS #5) and further in view of Goletz et al (U.S. Patent 5,997,869, issued 12/99) is withdrawn in view of the new grounds of rejection.

8. The rejection of claims 22-25 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention is withdrawn in view of the amendments to the claims.

9. The rejection of claims 22-25 under 35 U.S.C. 102(b) as being anticipated by Madiyalakan et al (WO 97/42973, published 11/20/97, IDS #5) is withdrawn in view of the amendments to the claims.

10. The rejection of claims 22-25 under 35 U.S.C. 102(e) as being anticipated by Madiyalakan et al (U.S. Patent 6,241,985, filed 3/20/98, IDS #5) is withdrawn in view of the amendments to the claims.

The following is a NEW GROUND of rejection

Claim Rejections - 35 USC § 103

11. Claims 22-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Madiyalakan et al [a] (WO 97/42973, published 11/20/97, IDS #5) or Madiyalakan et al [b] (U.S. Patent 6,241,985, filed 3/20/98, IDS #5) and further in view of Goletz et al (U.S. Patent 5,997,869, issued 12/99) and Madiyalakan et al [c] (Hybridoma 16:41-45, 1997) and Ma et al (Cancer Immunol. Immunother. 47:13-20, 1998).

The claims recite a method for diagnosing the efficacy of xenotypic antibody mediated immunity comprising measuring the level of a T cell response produced prior to administration of a murine monoclonal antibody to CA125 and measuring an increase in at least 1.5 fold in the T cell response after administration wherein the T cell response is a T helper response and a cytotoxic T cell response, wherein the increase is indicative of a favorable diagnosis of efficacy.

Madiyalakan et al [a] and [b] teach administration of a mouse monoclonal antibody directed to CA125 which is Mab-B34.13 which lead to an increase in cytotoxic T lymphocytes in human cancer patients (see Examples 2 and 8) and stimulates both a humoral and cellular response and administration of the xenotypic antibody led to an increase in the mean survival of the patients (see example 8). Madiyalakan et al [a] and [b] also teach the CA125 antigen fails to be recognized by the immune system and as such there would be no T cell response prior to administration. Madiyalakan et al [a] and [b] do not specifically teach measuring the T cell response prior to administration, or a 1.5 fold increase. These deficiencies are made up for in the teachings of Goletz, Madiyalakan et al [c], and Ma et al.

Goletz et al teach methods to immunize humans to induce cytotoxic T lymphocytes. Goletz et al teach as a preliminary step to determine the T cell response prior to administration of an agent (see column 15, lines 41-44).

Madiyalakan et al [c] teach administration of Mab-B43.13 to patients and the patients had an increase in IFN-gamma and patients that had increased survival had increased levels of IFN-gamma compared to preinjection levels and INF-gamma increased the ovarian tumor sensitivity to cytotoxic T cells and that patients injected with Mab-B43.12 have increased IFN-gamma in there sera and that IFN-gamma could improve the tumor sensitivity to CA125-specific cytotoxic T lymphocytes and IFN-gamma led to at least a 1.5 fold increase in ovarian tumor cell lines to cytotoxicity of CTLs (see page 43, 44 and abstract).

Ma et al teach induction of T cell response after administration of Mab-B43.12 and the T cell proliferation was any where from two to eight times higher than controls (see page 18, Figure 5, and abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have determined the T cell response prior to administration of the xenotypic antibody and after administration and used an increase in at least 1.5 fold as an indication of a favorable diagnosis of efficacy in view of the teachings of Madiyalakan et al [a], Madiyalakan et al [b], Madiyalakan et al [c], Goletz et al, and Ma et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have determined the T cell response prior to administration of the xenotypic antibody and after administration and used an increase in at least 1.5 fold as an indication of a favorable diagnosis of efficacy in view of the teachings of Madiyalakan et al [a], Madiyalakan et al [b], Madiyalakan et al [c], Goletz et al, and Ma et al because Madiyalakan et al [a] and Madiyalakan et al [b] both teach method for stimulating a cytotoxic T cell response and after administration of the xenotypic antibody a CTL response was generated and the generation of the CA125-specific CTLs led to increased survival (see example 8 and 9). In addition, One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have determined the T cell response prior to administration of the xenotypic antibody and after administration and used an increase in at least 1.5 fold as an indication of a favorable diagnosis of efficacy in view of the teachings of Madiyalakan

et al [a], Madiyalakan et al [b], Madiyalakan et al [c], Goletz et al, and Ma et al because Goletz et al teach that a preliminary step can be performed to determine the CTL response prior to immunization. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have determined the T cell response prior to administration of the xenotypic antibody and after administration and used an increase in at least 1.5 fold as an indication of a favorable diagnosis of efficacy in view of the teachings of Madiyalakan et al [a], Madiyalakan et al [b], Madiyalakan et al [c], Goletz et al, and Ma et al because Madiyalakan et al [c] teach prolonged survival after administration of Mab-B43.13 and an increase in IFN -gamma and increased cytotoxic cellular T cell responses after administration. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have determined the T cell response prior to administration of the xenotypic antibody and after administration and used an increase in at least 1.5 fold as an indication of a favorable diagnosis of efficacy in view of the teachings of Madiyalakan et al [a], Madiyalakan et al [b], Madiyalakan et al [c], Goletz et al, and Ma et al because Ma et al teach administration of Mab-B43.13 leads to T cell response of between two to eight fold and activated T cell s are known to have increased IFN-gamma (see page 18). Thus, it would have been obvious that an increase in at least 1.5 fold in a T cell response after antibody administration vs. prior would be indicative of a favorable outcome because Ma et al teach an increase in T cell response of two to eight fold with production of IFN-gamma and that a specific T cell response was seen after administration of the Mab-B43.13 and Madiyalakan et al [c] teach induction of IFN-

gamma in patients after administration of Mab-B43.13 and the IFN-gamma improved tumor cell sensitivity to CTLs and there was an increase of 2 fold in the T cell response (see page 44) and Madiyalakan et al [a], [b], and [c] each teach increased survival of patients after Mab-B43.13 administration and the tumor cells were more sensitive to CTLs after administration and it would have been obvious to obtain an increase in a T cell response because Ma et al teach "It is therefore important to design cancer vaccines for T cell mediated immunity" (see page 19). Thus, one would look for an increase in the T cell response after administration of the antibody of at least 1.5 fold.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

The response filed 7/30/03 has been carefully considured but is deemed not to be persuasive. The response states that claim 22 has been amended such that an increase in at least 1.5 fold in a T cell response in indicative of a favorable response and Neither Madiyalakan et al (WO 97/42973) or Goletz et al teach at least a 1.5 fold increase (see page 6-9 of response). In response to this argument, the references added to the 103 rejection make it obvious to look for a 1.5 fold increase in the T cell response as a favorable response.

Conclusion

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879